If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 415-576-0200.

Respectfully submitted,

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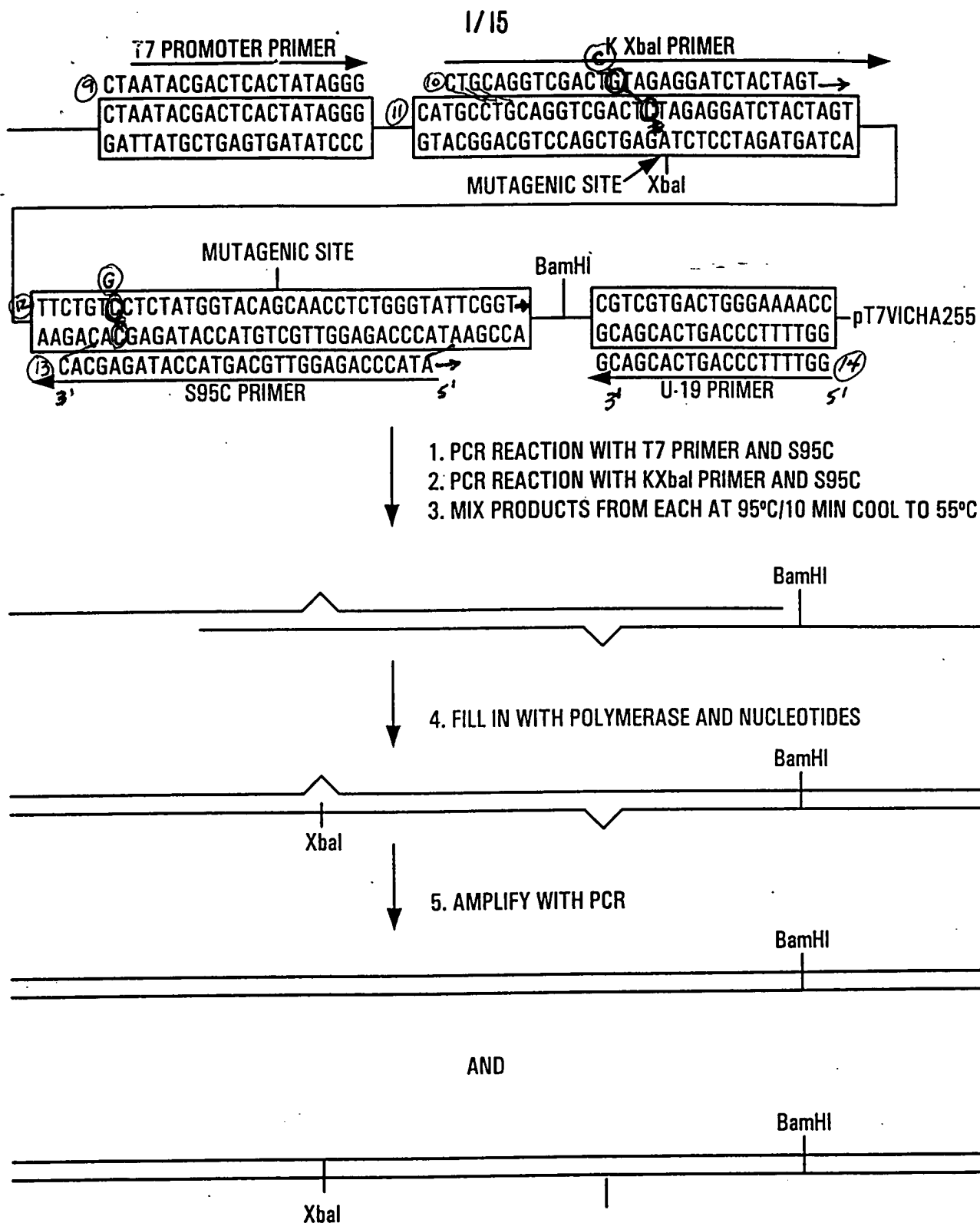Fax: (415) 576-0300
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T7 PROMOTER PRIMER

⑨ CTAATACGACTCACTATAGGG

K Xbal PRIMER

⑩ CTGCAGGTCGACTGTAGAGGATCTACTAGT→

| CTAATACGACTCACTATAGGG | ⑪ | CATGCCTGCAGGTCGACTCTAGAGGATCTACTAGT |
| GATTATGCTGAGTGATATCCC | | GTACGGACGTCCAGCTGAGATCTCCTAGATGATCA |

MUTAGENIC SITE   Xbal

MUTAGENIC SITE

G

BamHI

⑫ TTCTGTCCTCTATGGTACAGCAACCTCTGGGTATTCGGT→

AAGACAGGAGATACCATGTCGTTGGAGACCCATAAGCCA

⑬ CACGAGATACCATGACGTTGGAGACCCATA→
3'   S95C PRIMER   5'

| CGTCGTGACTGGGAAAACC | pT7VICHA255
| GCAGCACTGACCCTTTTGG |

GCAGCACTGACCCTTTTGG ⑭
3'   U-19 PRIMER   5'

1. PCR REACTION WITH T7 PRIMER AND S95C
2. PCR REACTION WITH KXbal PRIMER AND S95C
3. MIX PRODUCTS FROM EACH AT 95°C/10 MIN COOL TO 55°C

BamHI

4. FILL IN WITH POLYMERASE AND NUCLEOTIDES

BamHI

Xbal

5. AMPLIFY WITH PCR

BamHI

AND

BamHI

Xbal

FIG. 1.

XhoI

GGTGCTC

```
                    GAG TCT GGG GGA GAC TCA GTG
GAA GTG ACG CTG GTG  GAG TCT GGG GGA GAC TCA GTG  AAG CCT GGA GGG TCC CTG AAA CTC
CTT CAC TGC GAC CAC  CTC AGA CCC CCT GTG CAC      TTC GGA CCT CCC AGG GAC TTT GAG
Glu Val Thr Leu Val  Gly Ser Gly Gly Asp Ser Val Lys Pro Gly Gly Ser Leu Lys Leu
└─FR1
```

```
                                    G   G
TCC TGT GCA GCC TCT GGA TTC ACT TTA AGT GGT GAA ACC ATG TCT TCG CGC CAG ACT
AGC ACA CGT CGG AGA CCT AAG TGA AAT TCA CCA CTT TGG TAC ACA ACC GCG GTC TGA
Ser Cys Ala Ala Ser Gly Phe Thr Leu Ser  Gly Glu Thr Met Ser  Trp Val Arg Gln Thr
                              └─CDR1                              └─FR2
```

```
                        G                           G
CCG GAG AAG AGG CTG GAC  TGG GTC GCA ACC ACT CTT AGT GGT GGT TTC ACC TTC TAT
GGC CTC TTC TCC GAC CTG  ACC CAG CGT TGG TGA GAA TCA CCA CCA AAG TGG AAG ATA
Pro Glu Lys Arg Leu Glu  Trp Val Ala  Thr Thr Leu Ser Gly Gly  Phe Thr Phe Tyr
                                     └─CDR2
```

```
                            G                           C G
TCA GCC AGT GTG AAG GGT CGT TTC ACC ATC TCC AGA GAC AAT GCC CAG AAC AAC GTC TAT
AGT TCA CCG TCA CAC TTC CCA AAG TGG TAG AGG TCT CTG TTA CGG GTC TTG TTG GAG ATA
Ser Ala Ser Val Lys Gly  Arg Phe Thr Ile Ser Arg Asp Asn Ala Gln Asn Asn Leu Tyr
                       └─FR3
```

FIG. 2A.

CTA CAA CTG AAT AGT CTG AGG TCT GAG GAC ACG GCC TTG TAT TTC TGT GCA AGT CAT CGG
GAT GTT GAC TTA TCA GAC TCC AGA CTC TGC CGG ATA AAG ACA CGT TCA GTA GCC
Leu Gln Leu Asn Ser Leu Arg Ser Glu Asp Thr Ala Leu Tyr Phe Cys Ala Ser His Arg
|——COR3

CCCG GAGG
L ApaI

AGA CGT CGG TTT TGC TG→ GCA TCT GCA GCC AAA ACG ACA CCC CCA
TTT GTT CAC TGG GGC CAC GGG ACT CTG GTC ACT GTC TCT GCA GCC AAA ACG ACA CCC CCA
AAA CAA GTG ACC CCG GTG CCC TGA GAC CAG TTT TCC TGT CCT
Phe Val His Trp Gly His Gly Thr Leu Val Thr Val Ser Ala Ala Lys Thr Pro Pro
|——FR4 |——CH1

FIG. 2B.

SstI
XhoI

```
c    G Gc
GTCACACGTC
```

```
GCT GTT GTG ACT CAG GAA TCT GCA CTC ACC ACA TCA CCT GGT GAA ACA GTC ACT CTC ACT
CGA CAA CAC TGA GTC CTT AGA CGT GAG CCA TGT AGT GGA CTT TGT CAG TGT GAG TGA
Ala Val Val Thr Gln Glu Ser Ala Leu Thr Thr Ser Pro Gly Glu Thr Val Thr Leu Thr
                                                              FR1
```

```
                        G
TGT CGC TCA AGT ATT CGG GCT GTT ACA ACT AGT AAC TAT GCC AAC TGG GTC CAA GAA AAA
ACA GCG AGT TCA TAA GCC CGA CAA CGT TCA TGA TCA TTG CGG ACC CAG GTT CTT TTT
Cys Arg Ser Ser Ile Gly Ala Val Thr Thr Ser Asn Tyr Ala Asn Trp Val Gln Glu Lys
    CDR1                                                  Asn|Trp  FR2
```

```
CCA GAT CAT TTA TTC ACT GGT CTA ATA GGT GGT ACC AAT AAC CGG GCT CCG GGT GTT CCT
GGT CTA GTA AAT AAG TGA CCA GAT TAT CCA TGG TTA TTG GCC CGA GGC CCA CAA GGA
Pro Asp His Leu Phe Thr Gly Leu Ile Gly Gly Thr Asn Asn Arg Ala Pro Gly Val Pro
                              Gly|Gly                          Ala Pro|Gly  FR3
                              CDR2
```

```
GCC AGA TTC TCA GGC TCC CTG ATT GGA GAC AAG GCT GCC CTC ACC ATC ACA GGG GCA CAG
CGG TCT AAG AGT CCG AGG GAC TAA CCT CTG TTC CGA CGG GAG TGG TAG TGT CCC CGT GTC
Ala Arg Phe Ser Gly Ser Leu Ile Gly Asp Lys Ala Ala Leu Thr Ile Thr Gly Ala Gln
```

FIG. 3A.

ACT GAA GAT GAG GCA AGA TAT TTC TGT GCT CTA TCG TAC TGC AAC CTC TGG GTG TTC GGT
TGA CTT CTA CTC CGT TCT ATA AAG ACA CGA GAT ACG ATG TTG GAG ACC CAC AAG CCA
Thr Glu Asp Glu Ala Arg Tyr Phe Cys Ala Leu Trp Tyr Cys Asn Leu Trp Val Phe Gly

CDR3   FR4

GGA GGA ACC AAA CTG ACT GTC CTA AGC CAG CCC AAG TCT TCG CCA TCA GTC ACC CTG TTT
CCT CCT TGG TTT GAC TGA CAG GAT TCG GTC GGG TTC AGA AGC GGT CAG AGT TGG GAC AAA
Gly Gly Thr Lys Leu Thr Val Leu Ser Gln Pro Lys Ser Ser Pro Ser Val Thr Leu Phe

TTT GAC TGA CAG GAT TCG
Phe Asp

BsiWI
BalWI
CGTACGCTC

CCG CCC TCC TCT GAA GAG CTA AGC TTG GGA ATC GGA TTC CCG GG
GGC GGG AGG AGA CTT CTC GAT TCG AAC CCT TAG CCT AAG GGC CC
Pro Pro Ser Ser Glu Glu Leu Ser Leu Gly Ile Gly Phe Pro Gly

FIG. 3B.